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EXAMINER	
KERR, KATHLEEN M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,217	LEADLEY ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *4,5,13-29,35,36 and 39-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-12,30-34,37,38,46 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (mailed on April 6, 2004), Applicants filed an election received on June 7, 2004. Thus, Claims 1-47 are pending in the instant Office action.

Election

2. Applicant's election with traverse of Group 13, Claims 1-3, 6-12, 30-34, 37, 38, 46 and 47, in the reply filed on June 7, 2004 is acknowledged. The traversal is on the ground(s) that the restriction is improper because the Examiner failed to comply with the relevant portions of the M.P.E.P. § concerning unity of invention. This is not found persuasive because the Examiner did follow unity of invention restriction practice. While the unity of invention set forth in the restriction requirement did not match the unity of invention set forth in the International phase of the application, this is not required by the M.P.E.P. What is required is that unity be considered in the instant application view of a special technical feature might be shared by the invention(s). As set forth previously by the Examiner, the technical feature of Group 1 is not shared by the other product Groups because the feature is based on structure and, thus, is not a special technical feature.

Applicant further argues that at least Groups 10-15, 20, and 21 should be examined together under unity of invention because they are related in function and share a single inventive concept. The Examiner disagrees. To share an inventive concept, the Groups must share a special technical feature. The feature by which these Groups are claimed is structure.

Groups 10-15, 20, and 21 share a common general PKS gene structure, but the general PKS structure does not contribute to the prior art as a general theme, and, thus, cannot be considered a special technical feature. Groups 10-15, 20, and 21 do not share a common specific structure (DNA sequence). In addition to not sharing structure that can be considered a special technical feature, these Groups do not share the same function. While they are all drawn to DNAs encoding multienzymes involved in monensin biosynthesis, said enzymes catalyze distinct steps of the biosynthesis and, thus, have different functions as well as different structures.

The requirement is still deemed proper and is therefore made FINAL. Claims 1-47 are pending. Claims 4, 5, 12-29, 35, 36, and 39-44 are withdrawn from further consideration as non-elected inventions. Claims 1-3, 6-12, 30-34, 37, 38, 46 and 47 will be examined herein.

Priority

3. The instant application is granted the benefit of priority for the International Application No. PCT/GB00/02072 filed on May 30, 2000 and for the foreign application 9912563.5 filed on May 28, 1999 as requested in the declaration, which foreign application discloses the full-length gene cluster but not the negative limitation in Claim 1.

Information Disclosure Statement

4. No information disclosure statement has been filed with the instant application as of the date mailed of the instant Office action. Applicants are reminded that they have a duty to disclose all information, of which they are aware, relevant to the patentability of the pending claims (see 37 C.F.R. § 1.56 and M.P.E.P. § 2000).

Compliance with the Sequence Rules

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to **fully** comply with the requirements of 37 C.F.R. § 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

a) On page 44, lines 17-18, two oligonucleotides are disclosed without benefit of SEQ ID NOs.
b) On page 45, lines 11-12, two oligonucleotides are disclosed without benefit of SEQ ID NOs.
c) On page 51, lines 4-5, two oligonucleotides are disclosed without benefit of SEQ ID NOs.
d) On page 51, lines 18-19, two oligonucleotides are disclosed without benefit of SEQ ID NOs.
e) On page 52, lines 6-7, two oligonucleotides are disclosed without benefit of SEQ ID NOs.
f) On page 56, lines 13-14, two oligonucleotides are disclosed without benefit of SEQ ID NOs.
g) On page 56, lines 24-25, two oligonucleotides are disclosed without benefit of SEQ ID NOs.
h) On pages 68-69 (Table I), the SEQ ID NOs to which the "start" and "end" nucleotides refer must be clear. This is particularly relevant due to the division of the gene cluster among SEQ ID NOs:1-4.
i) On pages 70-99 (Table II), the amino acid sequences listed must be described by SEQ ID NOs. The Examiner suggests, however, that Applicant delete pages 70-99 and insert a new Table II that would contain all the information in pages 70-99 except the actual sequences, which are complete in the sequence listing.

If the noted sequences are in the sequence listing as filed, Applicants must amend the specification to identify the sequences appropriately by SEQ ID NO. If the noted sequences are not in the sequence listing as filed, Applicants must provide (1) a substitute copy of the sequence listing in both computer readable form (CRF) and paper copy, (2) an amendment directing its entry into the specification, (3) a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4) any amendment to the specification to identify the sequences appropriately by SEQ ID NO.

Objections to the Specification

6. The specification is objected to because the title is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are drawn (see M.P.E.P. § 606.01). The Examiner suggests the following new title:

---DNA Encoding MonAIV of the Monensin Polyketide Synthase Gene Cluster from *Streptomyces cinnamonensis*---

7. The specification is objected to for lacking a titled section to describe the figures. On page 21, the figures are described; this section must be titled ---Brief Description of the Drawings---. Correction is required.

8. The specification is objected to for having incomplete citations:

a) On page 40, line 1, the reference to "Messing, 1982" is incomplete. If a complete reference is found elsewhere in the specification as originally filed, the complete reference must be inserted here.

Correction is required.

9. The amendment filed November 28, 2001 is objected to under 35 U.S.C. § 132 because it introduces new matter into the disclosure. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: in Claims 22 and 26, the limitation of "a polyketide other than monensin".

Applicant is required to cancel the new matter in the reply to this Office Action or to cite clear support in the international application, as originally filed, for the added limitation.

10. The specification is objected to for being confusing with respect to the sequence listing. The sequence listing, filed on May 6, 2002, contains 52 sequences. No SEQ ID NOs are noted in the specification. It is unclear why said sequences are in the sequence listing if they are not described in the specification. All SEQ ID NOs in the sequence listing must be described in the specification. Appropriate correction is required.

Claim Objections

11. Claims 1-3, 6-12, 30-34, 37, 38, 46, and 47 are objected to for containing non-elected subject matter. All claims must contain all or a portion of the MonAIV gene. Correction is required.

12. Claim 1 is objected to for improper punctuation. The comma after "80%" should be removed.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 6-7 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 6, the phrase "polypeptides set out below" does not have antecedent basis below since the "table" referred to describes "peptide" and not ---polypeptides---. Correction is required.

14. Claims 6-7 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 6, the activity of "polyketide synthase multienzyme" is not an activity but a name. Thus, the functional requirement is unclear. The activities, as described in Figure 3, for MonAIV are ketosynthase activity, acyl transferase activity, dehydratase activity, ketoreductase activity, acyl-carrier protein activity, and enoyl reductase activity; however, these limitations cannot be read into the claims. These activities would also clarify the phrase "single enzyme activity of the multienzyme" in Claim 7. Clarification is required.

15. Claim 11 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear what a "corresponding polypeptide" refers to. Is this the encoded polypeptide? Moreover, not all of SEQ ID NOs:1-4 (the full length gene cluster) encodes protein because there are nucleotides between the open reading frames as disclosed in Table I. Clarification is required.

16. Claims 30-34 and 37-38 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 30, the abbreviation "PKS" is used without definition. An abbreviation must be defined upon its first appearance in the claims. The Examiner suggests replacing the term with ---polyketide synthase (PKS)--- for clarity.

17. Claims 30-34 and 37-38 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In line 7 of Claim 30, the phrase "said modules or a domain" in unclear if it refers to any PKS module, as described in line 2 of the claim, or if it refers to the immediately preceding occurrence in line 5, which is specific for monensin modules/domains. Clarification is required.

18. Claims 30-34 and 37-38 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 30, line 8, the phrase "an ery loading module" is unclear since the Examiner knows of only a single example of an erythromycin PKS with a single loading module. The article "an" indicates *any* (one of more than one) erythromycin loading module. Moreover, the abbreviation "ery" must be spelled out as erythromycin (or the well-known abbreviation DEBS) for clarity. Clarification is required.

19. Claims 30-34 and 37-38 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 30, the abbreviation "AT" is used without definition. An abbreviation must be defined upon its first appearance in the claims. The Examiner suggests replacing the term with ---the acyl transferase (AT) domain --- for clarity.

20. Claim 34 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

the invention. The phrase "derived from" is unclear. Must the loading module be the disclosed monensin loading module? If not, what kind of changes does "derived from" allow? Clarification on the metes and bounds of the phrase is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

21. Claims 1-2, 8-12, 46 and 47 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to a DNA product that is either a portion of the full-length MonAIV gene or a variant having a particular % sequence identity to the MonAIV gene (or its encoded protein) wherein said fragments and variants have open claim language and lack a requisite function.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed

genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

The instant specification teaches SEQ ID NOs:1-4 that together make up the entirety of the monensin gene cluster of 103,600 nucleotides. Large portions of SEQ ID NOs:1-4 encode proteins involved in the biosynthesis of monensin as disclosed in Table I. Each of the proteins involved has a distinct function, whether that be a methyl transferase and a monensin resistance gene, both considered "accessory proteins", or MonAI and MonAII, which catalyze analogous, but distinct reactions (note different "substrate" as pictured in Figure 3 of the instant application). The instant specification describes the genus relating to said SEQ ID NOs with both sequence identity (or fragment) limitations and functional limitations. However, the genus of the instant claims also contains polynucleotides within the sequence identity (or fragment) limitations, but having different function. Applicants have not fully described a genus that has sequence identity limitations in the absence of functional limitations.

22. Claims 3, 6, and 7 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 3 is drawn to DNA sequence that is claimed without any structural limitations; the terms "allele, mutation, or other variant" have no specifically defined breadth and, thus, cannot be considered to structurally limit

the claimed subject matter. The functional limitation of "encoding ... one polypeptide which is necessary for the biosynthesis of monensin" is not a universally applicable limitation by virtue of the phrase "at least a part of" which can be as small as one amino acid residue of the polypeptide, thus, not limiting whatsoever.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, the MonAIV gene is described as nucleotides 42448-54564 (SEQ ID NO:2 from 12448-24564) that encodes a 4039 amino acid protein that is a polyketide synthase multienzyme having domains as described in Figure 3 (see also Tables I and II). Due to the lack of structural limitation in the claims, the DNA is only limited according to the functional characteristics of the enzyme it encodes, as implied by "encoding ... a polypeptide ... for the biosynthesis of monensin". Therefore, the claimed DNA can have any structure while retaining

the implied function. Thus, one of skill in the art would be unable to predict the structure of other members of this genus by virtue of the instant disclosure.

23. Claims 30-34 and 37-38 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 30 is drawn to a DNA that is claimed solely by function, by virtue of encoding PKS and/or monensin modules/domains and without any structural limitations.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

The generic term "polyketide synthase" has developed in the art such that its name garners a description of its structure and function. Thus, the term "DNA encoding ... one PKS

loading module and ... PKS extension modules" is adequately described in view of the specification and the prior art such that one of skill in the art would be able to predict the general structure and function of other members of the claimed genus. When this term of art is limited to "monensin module or domain", the generic description of structure and function in the art no longer suffices to support claimed subject matter because one of skill in the art cannot predict the structure of such a DNA sequence. The Examiner suggests using specific structure/function language (such as percent identity) in the claims.

24. Claims 1-3, 6-12, 30-34, 37, 38, and 46-47 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for any DNA encoding the 4039 amino acid sequence described as MonAIV in Table II, does not reasonably provide enablement for DNA of fragments and/or as little as 80% sequence identity to such DNA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To make the claimed invention to the full extent of its scope would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is

needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The instant application presents no guidance or working examples of the use of polynucleotides that have such low sequence identity with respect to SEQ ID NO:2 (12,448-24,564). The art fully enables any DNA encoding said sequence based on the degeneracy of the genetic code. While the art teaches numerous examples of general PKS gene clusters, no other specific examples of monensin gene clusters are known. The nature of the invention is such that the DNA encodes a functional protein, a polyketide synthase containing several PKS domain having PKS enzyme activities useful in the biosynthetic pathway of monensin; and with such a great deviation from the known sequence, the predictability of functionality becomes extremely low. Such enormous breadth and unpredictability renders the instant claims not enabled to the full extent of their scope without undue experimentation. Moreover, while the instant specification describes and enables means for identifying other monensin PKS genes using hybridization methods and functional screening, etc., these methods do not enable one of skill in the art to make all, or a relevant portion of, the polynucleotides within the scope of the claims because the ability to find a monensin PKS gene, which is structurally related to SEQ ID NO:2,

is not equivalent to the ability to make a monensin PKS gene as required by the statute (i.e., "make and use"). No description in the specification or the art provides particular residues whose encoding is important within the disclosed sequence so that its monensin PKS-nature is maintained. Thus, one of skill in the art would be unable to predict the structure of the other members of the genus in order to make such members. Therefore, the instant claims are not enabled to the full extent of their scope.

Claim Rejections - 35 U.S.C. § 101

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

25. Claims 1-3, 6-9, 46, and 47 are rejected under 35 U.S.C. § 101, utility, because the claimed invention is directed to non-statutory subject matter. The claims, as written, do not sufficiently distinguish over DNA as they naturally exist because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206, USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of "isolated" or "purified" as taught by the specification. See M.P.E.P. § 2105.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

26. Claims 1, 3, 6-10, 12 and 47 are rejected under 35 U.S.C. § 102(b) as being anticipated by GenBank Accession Number AF144047 (*Streptomyces cinnamonensis* macrolide type polyketide synthase gene, partial cds. July 12, 1999). The instant claims are drawn to a DNA comprising a part of the MonAIV gene, which is SEQ ID NO:2, 12,448-24,564 (also found in GenBank Accession Number AF440781 from 42448-54564). The instant claims are also drawn to variants of the MonAIV gene encoding enzymes having PKS activity a. The length of the DNA must be at least 60 bases.

GenBank Accession Number AF144047 teaches a 740 base pair *Streptomyces cinnamonensis* sequence from described as encoding a macrolide type polyketide synthase, wherein said sequence aligns with two portions of MonAIV as shown in the attachment. The largest contiguous portion of the match is 21 base pairs; however, the length requirement is met by the overall length of the sequence (the limitation does not require a fragment of SEQ ID NO:2 (MonAIV). A cloning vector is inherent in the GenBank disclosure.

27. Claims 1-3, 6-10, 12 and 47 are rejected under 35 U.S.C. § 102(b) as being anticipated by GenBank Accession Number U78289 (*Streptomyces fradiae* tylactone synthase, started modules and modules 1-7, (tylG) gene, complete cds. August 13, 1997). The instant claims are drawn to a

DNA comprising a part of the MonAIV gene, which is SEQ ID NO:2, 12,448-24,564 (also found in GenBank Accession Number AF440781 from 42448-54564). The instant claims are also drawn to variants of the MonAIV gene encoding enzymes having PKS activity. The length of the DNA must be at least 60 bases. The instant claims are also drawn to a variant of a monensin PKS gene cluster.

GenBank Accession Number U78289 teaches a 43280 base pair sequence described as encoding a complete tylactone synthase, which is known in the art as a polyketide synthase, wherein said sequence aligns with several portions of MonAIV as shown in the attachment. Tylactone synthase can be considered a variant of monensin polyketide synthase. The largest contiguous portion of the match is 39 base pairs; however, the length requirement is met by the overall length of the sequence (see note above). A cloning vector is inherent in the GenBank disclosure.

28. Claims 11, 30-34 and 37-38 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kuhstoss *et al.* (Production of a novel polyketide through the construction of a hybrid polyketide synthase. Gene (1996) 183: 231-236). The instant claims are drawn to host cells transformed with a DNA sequence containing a part of (or a variant of) the MonAIV gene capable of expressing the encoded polypeptide. The instant claims are also drawn to hybrid DNA products containing at least one loading PKS module and more than on PKS extension module comprising variants of monensin modules wherein adjacent modules are not naturally contiguous, wherein said loading module is adapted to load a starter unit not normally received by the adjacent extender module.

Kuhstoss *et al.* teach hybrid PKS DNA molecules comprising the loading module of the tylactone PKS, a monensin variant (as described above), and extension modules of the platenolide I PKS (see Figure 3), which can also be considered a monensin variant. Kuhstoss *et al.* also teach transformation of said DNA molecules into *S. ambofaciens* host cells for expression and production of polyketides (see page 234, left column).

Conclusion

29. Claims 1-3, 6-12, 30-34, 37, 38, 46, and 47 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kathleen M Kerr
Examiner
Art Unit 1652

August 20, 2004